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Satiety Does Not Affect Gustatory Activity in the Nucleus of the Solitary Tract of the Alert Monkey

SIMON YAXLEY, EDMUND T. ROLLS, ZENON J. SIENKIEWICZ and THOMAS R. SCOTT*

University of Oxford, Department of Experimental Psychology, Oxford OX1 3UD (U.K.)

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Feeding to satiety decreases the acceptability of the taste of food. In order to determine whether the responsiveness of gustatory neurons in the nucleus tractus solitarius (NTS) is influenced by hunger, neural activity in the NTS was analyzed while monkeys were fed to satiety. Gustatory neural activity to glucose, fruit juice, NaCl, HCl and quinine HCl was measured before, while and after the monkey was fed to satiety with glucose, fruit juice or sucrose. While behavior turned from avid acceptance to active rejection upon repletion, the responsiveness of NTS neurons to the stimulus array, including the satiating solution, was unmodified. It is concluded that at the first central synapse of the taste system of the primate, neural responsiveness is not influenced by the normal transition from hunger to satiety. This is in contrast to the responses of a population of neurons recorded in the hypothalamus, which only occur to the taste of food when the monkey is hungry. Thus, NTS gustatory activity appears to occur independently of normal hunger and satiety, whereas hypothalamic neuronal activity is more closely related to the influence of motivational state on behavioral responsiveness to gustatory stimuli.

INTRODUCTION

There is evidence that the hypothalamus is involved in the control of feeding and drinking[2,16,17,21,34–36,45,52]. Part of this evidence is that there is taste-evoked neural activity in the hypothalamus and that this is related to motivation. Thus, several reports indicate that in the rat hypothalamus, gustatory neuronal activity is related to palatability[18,24], physiological need[9,10,54,55] and past experience[1]. In the monkey, the activity of single neurons is being recorded during normal feeding[34,45]. It has been found that a population of neurons in the lateral hypothalamus and adjoining substantia innominata respond to the sight and/or taste of food[40]. Part of the evidence that these neurons are involved in the control of the responses which are made to food when hungry is that they only respond to food when the monkey is hungry[6,47]. Indeed, it has been suggested that the principle whereby the sensory response to a motivationally relevant sensory stimulus such as the taste of food is modulated by the motivational state, for example hunger, is one important way in which motivational behavior is controlled[37].

Given that such modulation of sensory input by motivation is seen when recordings are made from hypothalamic neurons, it may be asked whether this is a special property of hypothalamic neurons which they show because they are involved in the control of motivational responses, or whether this type of modulation is a general property which is evident throughout sensory systems. In order to obtain evidence on this, in the experiments described here we recorded the activity of single neurons in the monkey in the first central relay in the gustatory system, the rostral part of the nucleus of the solitary tract[3,4], to determine whether neuronal responses here are influenced by motivational state. The recordings were made under the same conditions in which the responsiveness to gustatory stimuli of hypothalamic neurons

* Present address: Department of Psychology and Institute for Neuroscience, University of Delaware, Newark, DE 19716, U.S.A.
Correspondence: E.T. Rolls, University of Oxford, Department of Experimental Psychology, South Parks Road, Oxford OX1 3UD, U.K.

has been shown to be influenced by hunger, that is during feeding to normal satiety[6,47].

As recordings had not been made from neurons in the NTS previously in the behaving animal, and from neurons in the primate in the gustatory part of the NTS, we performed a first study, described elsewhere, in which we analyzed the responses of gustatory neurons in the monkey NTS[50]. In the study described here, we determined whether hunger influenced the responsiveness of neurons recorded in the nucleus of the solitary tract. The recordings were made in the monkey, to make the results as relevant as possible to understanding sensory processing and the control of feeding in man.

MATERIALS AND METHODS

The methods used were similar to those described previously[6,40–43,50] and are presented here only briefly, except where they differ.

Recording

Two male cynomolgus monkeys, *Macaca fascicularis*, weighing 3.8–4.0 kg were implanted under thiopentone sodium anesthesia with stainless-steel holders on which a Kopf adaptor could be fitted during recording sessions. After one or two weeks, daily recording sessions were initiated. Neuronal activity was recorded using glass-coated tungsten microelectrodes plated with gold and platinum black[19] while the monkey sat in a primate chair with head restraint to provide recording stability. The electrode was introduced into the brain through a guide tube whose tip was just below the dura, which was anesthetized with lignocaine. The electrodes were made as small as 1–2 μm in order to record from the small neurons in the gustatory part of the NTS. The signal from the microelectrode was passed through a FET source follower amplifier mounted on the microdrive, amplified by conventional band-pass filtered amplifiers and displayed on an oscilloscope. Since it was not possible to maintain functional contact with one NTS neuron for the 60–90 min duration of a satiety experiment, all recordings in this study were taken from small groups of NTS cells. Considerable care was taken to ensure the stability of the multiunit sample under study (see protocol below). The monkey was fed and given water ad libitum, at the end of each daily recording session, so that he was approximately 18 h food- and water-deprived during the recording sessions.

Stimuli and stimulus delivery

Five stimuli plus water were applied to the tongue during a recording session. Four were prototypes of the 4 basic tastes, each at a concentration determined by intensity–response functions in these same subjects[50]. These were 1.0 M glucose (0.3 M sucrose was substituted in one experiment), 1.0 M NaCl, 0.01 M HCl and 0.001 M quinine HCl. The 5th stimulus was 20% blackcurrant juice (Ribena, Beecham Products, Brentford, U.K.). This was chosen, because of its palatability and complexity of taste, as a stimulus which would be readily accepted and which would activate many gustatory neurons.

Stimuli were delivered through a hand-held syringe in quantities of approximately 0.5 ml. Manual delivery was used to ensure replicable gustatory stimulation of a large and nearly constant receptive field throughout a recording session despite different mouth and tongue positions adopted by the monkeys as the palatability of the solutions varied with the stimulus quality and level of satiety.

Gustatory neurons in the nucleus of the solitary tract responded differentially, but usually not uniquely, to the 4 prototypical taste stimuli. They could be clearly distinguished from nearby neurons with somatosensory responses, which altered their firing rates during touch to the mouth, mouth movements, and/or the ingestion of water (see ref. 50).

Requirements for conducting a satiety experiment

Ten satiety experiments were performed at different sites within the gustatory part of the NTS. Each was separated from the others by at least two days so as to permit the effects of repletion to dissipate. In order to initiate a satiety experiment, 3 conditions had to be satisfied.

(1) Gustatory responsiveness to the satiating chemical. The neural response elicited by application of the stimulus which would subsequently be used to satiate the monkey had to be robust. Since satiety was induced in most cases by glucose and in all cases by sweet stimuli, NTS chemotopography dictated that most recordings be made in the anterior part of the nucleus where sweet sensitivity is best[50].

(2) Recording stability. After a small group of responsive neurons had been found in the gustatory part of the NTS, the stability of the recording and of the evoked response were tested periodically over the next 30–60 min before a decision was made to begin the experiment. Approximately two-thirds of the potential sites for satiety experiments were rejected for reasons of inadequate stability. The difficulty of obtaining stable recordings in the NTS was due partly to movements of the brainstem and partly to the smallness of the cells.
(3) Avidness for the satiating chemical. A series of objective criteria for the avidness of acceptance has been developed[51]. A satiety experiment was not initiated unless a monkey's behavior warranted a rating of at least +1.0 on a scale of +2.0 (acceptance) to −2.0 (rejection) (see below). In practice this required an efficient search for the NTS and the achievement of a stable recording with a minimum of stimulus presentations, so that the monkey was still hungry when the experiment started.

Criteria for acceptance or rejection

Scores on the scale of acceptance or rejection were based on the following behavioral criteria:
+2.0: maximal acceptance; reaching for the solution with hands and mouth; avid licking.
+1.0: clear acceptance; opening the mouth, licking and swallowing the solution.
0.0: neutrality; swallowing the solution when placed in the mouth; absence of avidness; no attempt made to obtain the solution.
−1.0: clear rejection: pursing the lips to prevent administration of the solution; failure to swallow all of the solution placed in the mouth.
−2.0: maximum rejection: pursing the lips and closing the teeth; using the tongue to eject delivered solution; swallowing little; using the hands to push away the solution.

If the behavior was intermediate between these types, then intermediate scores were given.

Protocol

If the criteria for conducting a satiety experiment were satisfied, the following protocol was invoked.
(1) The gustatory neural response to each of the 5 sapid stimuli plus water was determined by application of 0.5 ml of each solution. Each application was followed by a 1.0 ml water rinse, and a minimum period of 30 s of rest. The stimulus series was then repeated. The total resting time was approximately 12 min, and the volume consumed was a maximum of 16 ml.
(2) The monkey's acceptance–rejection score for the satiating solution was determined by observing his response as 0.5 ml was applied to the tongue.
(3) The monkey was fed a 50 ml aliquot of the satiating solution. In 7 cases this was 20% w/v glucose. This was the primary agent for inducing satiety because, insofar as postabsorptive processes are involved, these will be expedited by glucose which needs not be metabolized before absorption. In one case 20% w/v sucrose was employed, and in two cases 20% blackcurrant juice, so as to provide a wider range of information on satiety. All satiating solutions were delivered by a syringe. The duration of administration was approximately two min for the initial aliquot, and as much as 4 min for the last.
(4) The monkey's acceptance–rejection score to the satiating solution was re-assessed.
(5) Steps 1–4 were repeated through as many cycles as were required to attain a behavioral score of −1.5 to −2.0. This typically involved five 50 ml aliquots over a period of 60 min. Conventional satiety, defined by the stage at which the subject would stop working to obtain food, would normally correspond to a rating of 0.0 to −0.5. Thus, the feeding used in these experiments was sufficient to produce very complete satiety, to ensure that if there was a modulation of the neuronal responses by satiety, the degree of satiety induced in the experiments was sufficient for the effect to be manifested. After satiety was reached, and feeding had stopped, multiple further measurements were taken of the neuronal responses to each of the sapid solutions and to water.

Analysis

Multiunit responses were acquired, analyzed and displayed on-line by a PDP-11 computer. Mean discharge rates were computed during either control periods or stimulus presentation, with the analysis extending 5 s from stimulus onset. Neuronal activity, together with stimulus markers, was also recorded on magnetic tape for subsequent analysis, which included the calculation and display of peristimulus time histograms in 50 ms bins.

Localization of recording sites

The position of each recording site was determined in two ways. First, following each track, X-ray photographs were taken from frontal and lateral perspectives. Recording sites could then be reconstructed to within 250 μm by reference to deep electrodes permanently implanted at planes close to those of the recording track. The positions of the deep electrodes were subsequently determined histologically. Second, in the final tracks, microlesions were made through the recording electrode (60 μA for 60 s, electrode-negative). After the final experiment, the tranquilization with ketamine was followed by a lethal i.v. dose of sodium pentobarbital. Perfusion was with 0.9% saline followed by formal-saline. The brains were placed in sucrose formalin for at least 7 days after which 50 μm serial frozen sections were cut and stained with cresyl violet and by the Gallyas[11] method for myelin (for which 25 μm sections were used).

RESULTS

The 10 sites at which satiety experiments were performed are shown in Fig. 1. They are within the boundary of the gustatory part of the NTS as delineated by autoradiographic tracing of gustatory afferent fibres[3,4], and are predominantly toward the rostral part of the gustatory region, as shown electrophysiologically[50].

The effects of feeding the monkey to satiety on the gustatory responses elicited by the satiating chemical are shown in Fig. 2. Each part of the figure shows one experiment, with the gustatory responses to the satiating chemical and the spontaneous firing rate, indicated at the different stages of each experiment. In 7 experiments the satiating chemical was glucose, in two cases blackcurrant juice, and in one case sucrose, as labelled. It is clear that in no case did satiety abolish, or even produce a major reduction in the respon-

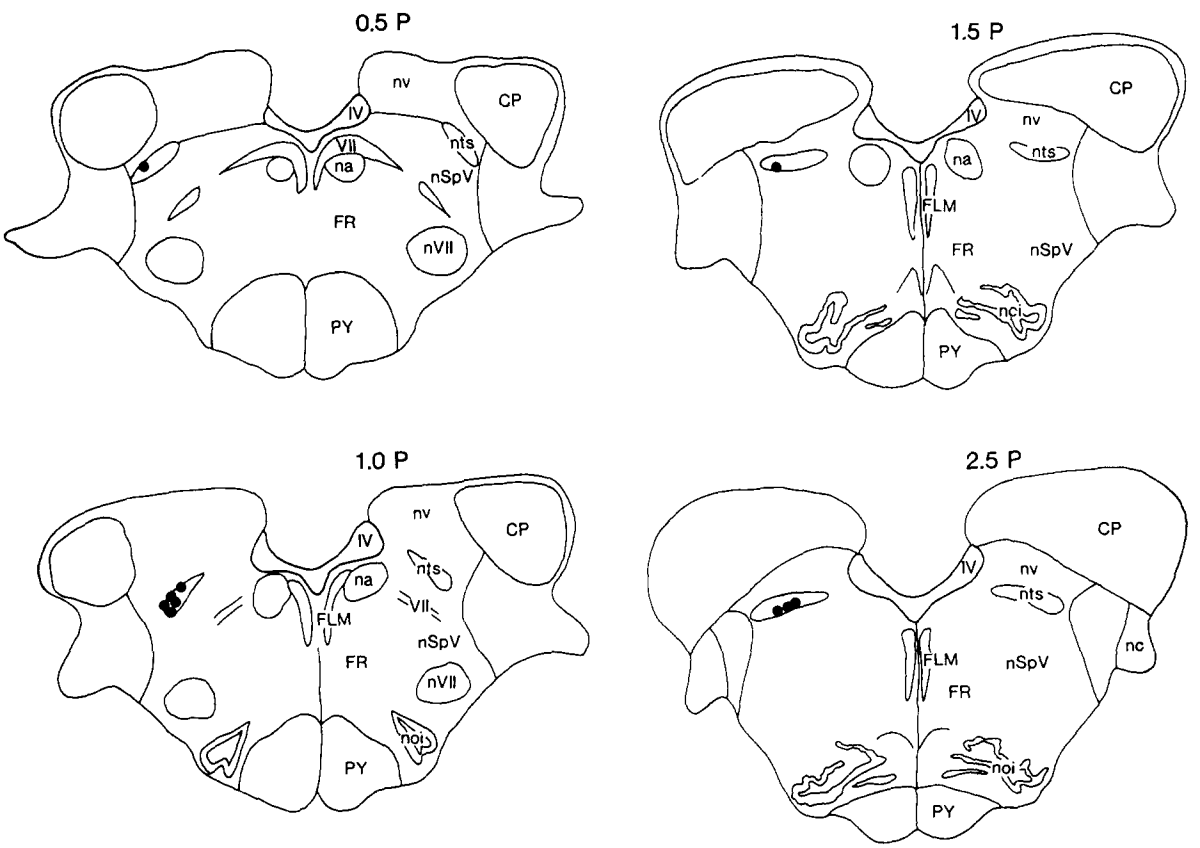

Fig. 1. The recording sites at which the 10 satiety experiments were performed. The calibrations refer to millimeters posterior to the auditory meatus. CP, cerebellar peduncle; FLM, fasciculus longitudinalis medialis; FR, formatio reticularis; na, nucleus abducens; nc, nucleus cochlearis; nSpV, nucleus tracti spinalis nervi trigemini; nts, nucleus tractus solitarius; nv, nucleus vestibularis; noi, nucleus olivaris; nVII, nucleus n. facialis; PY, pyramidal tract; IV, 4th ventricle; VII, nervus facialis (genu).

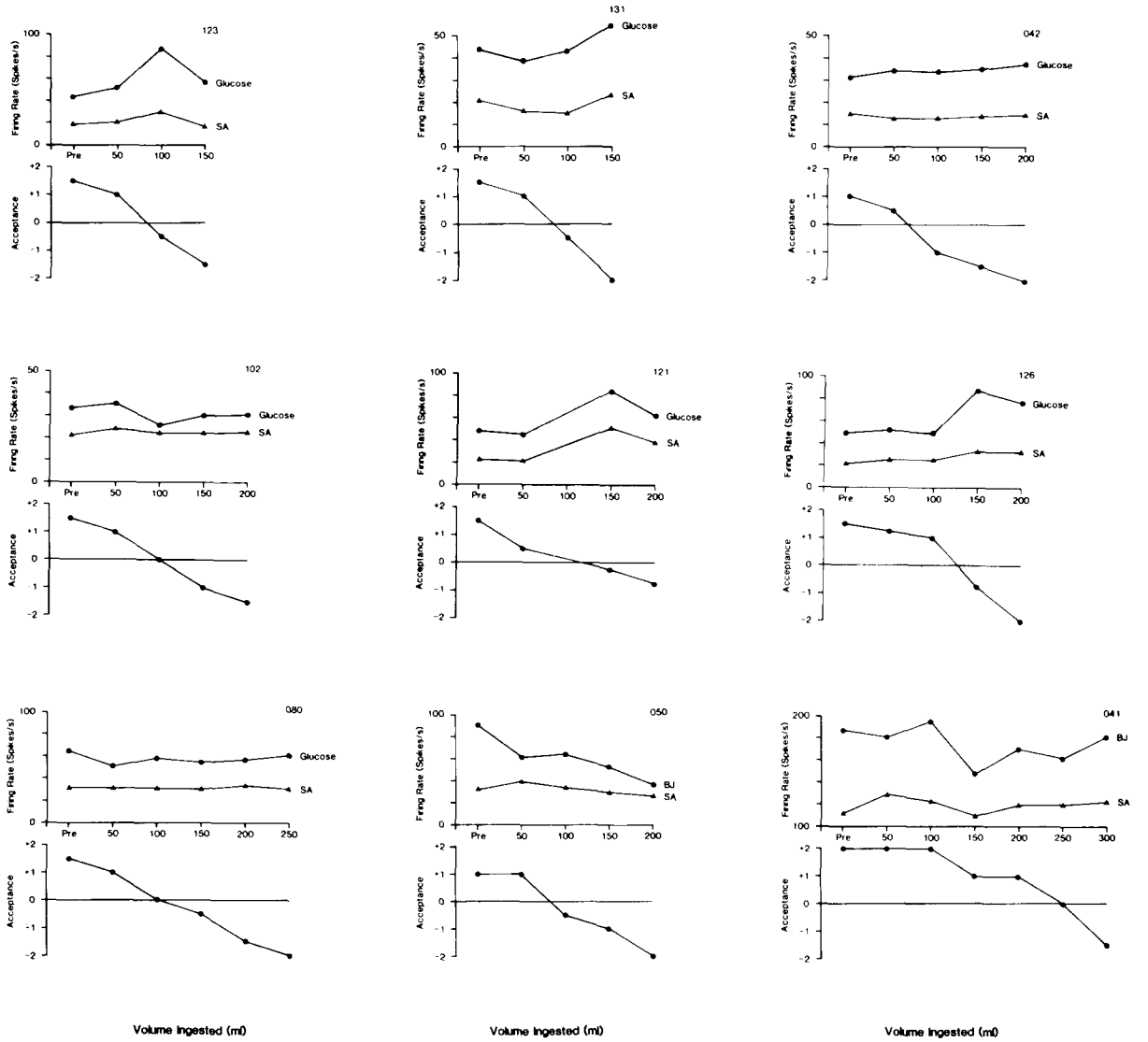

Fig. 2. Effects of feeding to satiety on the neural response (spikes/s) to the solution on which the monkey was satiated for 9 of the 10 separate experimental runs. The spontaneous firing rate is also indicated (SA). Below the neural response data for each experiment, the behavioral measure of the acceptance or rejection of the solution on a scale from +2 to −2 (see text) is shown. The solution used to feed to satiety is indicated. The monkey was fed 50 ml of the solution at each stage of the experiment, until he was satiated as shown by whether he accepted or rejected the solution. BJ, blackcurrant juice.

siveness of the neurons to the food. In 8 cases there was no statistically significant change in responsiveness to the satiating solution (t-test), in one case (050) there was a decrease to blackcurrant juice ($P < 0.01$), and in one case (121) there was an increase to glucose ($P < 0.05$). The changes of firing rate observed in these last two experiments probably do not reflect modulation of sensory responsiveness by satiety for at least two reasons. First, they indicate opposite results with the same experimental manipulation, and do so against a background of no significant changes in the other 8 experiments. Second, in both cases spontaneous activity (see Fig. 2) and the responses to several other gustatory stimuli and to distilled water, changed significantly in the same direction as did the response to the satiating solution. Thus, the alteration in the measured firing rate to the satiating stimulus probably only reflected a general

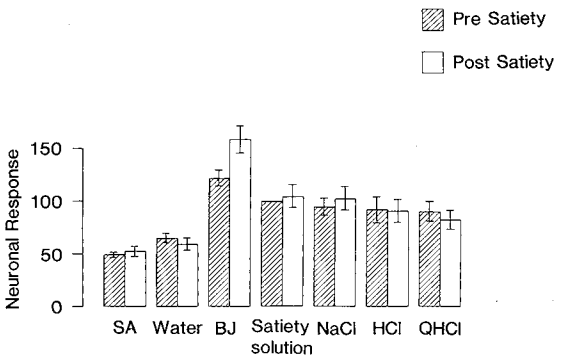

Fig. 3. The neuronal response before and after satiety to each of the gustatory stimuli and to the solution on which the monkey was satiated. The results are expressed relative to the response obtained to the solution on which the monkey was satiated before satiety (set at 100%) and the data are averaged over the 10 experimental runs, with the mean and S.E.M. shown. The satiating solution was 20% glucose in 7 cases, 20% sucrose in one case and blackcurrant juice in two cases. SA, spontaneous activity.

alteration of the number of spikes which entered the window of the trigger circuit, produced by for example slight electrode drift. Indeed, consistent with this, the ratio of the food to the non-food evoked gustatory response did not change in these cases (see below).

The results of feeding the monkey to satiety on the neural responses to each of the gustatory stimuli are shown in Fig. 3. The means and standard errors of the firing rates of the neurons before the satiety test was started, that is when the monkey was approximately 18 h food-deprived, and after the monkey had been fed to satiety, are indicated. The results are shown averaged over all 10 experiments in order to provide a summary of the effect of satiety on processing in the NTS. It is clear that no consistent changes in the gustatory responses to either the gustatory stimulus with which satiety was produced, or to any other of the gustatory stimuli used, were produced by feeding to satiety. Averaged over all 10 experiments, the effect of satiety was to increase the response to the food on which the monkey was satiated by 4%. This effect was not significant, as shown by a paired t-test which compared the response to the food before and after it was eaten to satiety ($t = 0.37$, $P > 0.7$, df = 9). Thus, overall, there was very little effect of the satiety on the responsiveness of these gustatory neurons.

Another way in which the effect of satiating the monkey on the neuronal responsiveness was analysed was by comparing the response to the satiating solution (food) to the responses to 1.0 M NaCl, 0.01 M HCl and 0.001 M quinine HCl (non-foods), before and after satiety. If satiety decreased the response to the food stimulus, but not to other gustatory stimuli, this ratio should decrease. This type of comparison made allowance for the possibility that the amount of neuronal activity in the triggering window changed after the experiment had been running for some time. The ratios of food to non-food responses showed no change as a result of satiety (mean before satiety 1.22, after satiety 1.22). Thus, this analysis also showed that satiety had little influence on the responsiveness of neurons in the NTS.

DISCUSSION

These results provide evidence that satiety does not modulate the responsiveness of gustatory neurons in the nucleus of the solitary tract of the monkey. It may be emphasized that this result was found under physiological conditions, when the monkey himself determined when he was satiated. Although apparent modulation of responsiveness may be demonstrable under artificial conditions, such findings may not reflect what actually occurs in normal, physiological, satiety.

Three possible ways in which an effect of satiety on gustatory responsiveness might have been undetected in these experiments are considered next. First, the affected neural population may have been limited to an area of NTS from which we did not record. This seems unlikely in that we sampled from 10 sites in two monkeys, and included the responses of perhaps 200 neurons. (This estimate of 20 cells in the typical multiunit record arises from the observations that the mean spontaneous firing rate of these neurons is 1.2 spikes/s, and the mean response evoked in single cells by the solutions used here is approximately 5.0 spikes/s — Scott, Yaxley, Sienkiewicz and Rolls, 1985. In the multiunit records of the present experiments, spontaneous activity averages 32 spikes/s and the mean evoked response is 62 spikes/s. Thus, it is estimated that the typical multiunit record included 12–27 neurons. In studies where artificially induced satiety has reduced taste-evoked activity in the rat NTS, nearly every multiunit site registered a decline[12,13]. Second, within a multiunit sample, it is

possible that reduced and augmented neuronal responses cancelled out each other. As unlikely as this seems, both on logical grounds and from the rat data[12,13], it is a possibility which can only be addressed by recordings from single neurons — and this is a difficult prospect in the NTS for the time period required to measure the neuronal responses and to induce satiety. Perhaps further rostral in the gustatory pathways, where recording stability should be greater, it will be more feasible to obtain recordings from single gustatory neurons while satiety is induced. Third, the results do not eliminate the possibility that at some considerable time into the post-satiety period, some decrease of responsiveness to foods might occur. But even if this does occur, such modulation would then not account for the change in acceptability of food, which of course is seen as the satiety develops, and is used to define satiety. Nor would this modulation be relevant to the decrease in the pleasantness in the taste of a food which occurs when it is eaten to satiety[7,8,31–33,41,45,46].

Thus, it appears that the reduced acceptance of food as satiety develops, and the reduction in its pleasantness, are not produced by a reduction in the responses of neurons in the nucleus of the solitary tract to gustatory stimuli. Sites at which neuronal responsiveness to the taste of food is modulated by satiety include the lateral hypothalamus and substantia innominata, and neurons in these regions may accordingly be more closely related to motivational control systems for feeding, and the effects which motivational state have on the palatability of food[6,36,39,45].

The implied dichotomy between quality–intensity coding in the NTS and hedonic–motivational coding in the diencephalon is consistent with a majority of psychophysical reports on the effects of satiety. Though there is some disagreement in the literature[14,15,49], humans often describe a significant decrease in the pleasantness of a food on which they have been satiated without a comparable decrease in its perceived intensity[22,23,46]. If the neural mechanisms for these effects are separate, such a result is understandable. More specifically, the separability of pleasantness and intensity sensations would not have been expected if at the first central synapse in the gustatory system, neuronal activity had been gated off by satiety.

The present results also provide evidence on the nature of the mechanisms which underlie sensory-specific satiety. Sensory-specific satiety is the phenomenon in which the decrease in the palatability and acceptability of a food which has been eaten to satiety are partly specific to the particular food which has been eaten[31–33,41,45–47]. The present results suggest that such sensory-specific satiety cannot be largely accounted for by adaptation at the receptor level, or by decreased responsiveness of peripheral gustatory nerves or of the NTS, to the food which has been eaten to satiety, otherwise modulation of neuronal responsiveness should have been apparent in the present study. This conclusion is consistent with analyses of sensory-specific satiety, in which it has been found that there can be a large decrease in the pleasantness of the taste of a food without the intensity of the taste of that food being severely attenuated[46]. Brain sites at which neuronal responses to gustatory stimuli parallel sensory-specific satiety include the lateral hypothalamus and substantia innominata[47], and neurons in these regions may accordingly be more closely related to the neural mechanisms which underlie sensory-specific satiety[36,39,45].

There is evidence that in the rat gastric distension and increases in blood glucose level can decrease neural responses in the gustatory NTS[12,13]. There is a number of possible reasons why different results were obtained in the rat from those described here for the monkey. First, the results from the monkey NTS were obtained from an alert animal feeding to normal self-determined satiety, whereas those from the rat reflect responsiveness under artificial conditions. For example, the blood glucose levels in the rat, which exceeded 200 mg%[12], may have been higher than those which occur normally (in the rat and monkey). Second, the rat studies were performed under anesthesia. Third, it is possible that the control systems for feeding operate differently in the rat and the primate. It does at least appear that the anatomy of the gustatory system is different in the rat and the monkey. In the rat, the gustatory NTS projects to the parabrachial nuclei from which fibers proceed both to the gustatory thalamus (medial ventrobasal complex) and directly to forebrain areas implicated in motivation such as the lateral hypothalamus, substantia innominata and amygdala[24–30]. The hypothalamus projects directly back to the NTS[5,49]. By con-

trast, in the monkey gustatory NTS projects exclusively to the thalamic taste relay[4,28] from which fibers pass to the gustatory cortex. A possible route for gustatory information to reach the hypothalamus is then via the insula and amygdala[20], or via the orbitofrontal cortex[52]. Thus, in the rat, it is possible that with the close interconnection of the NTS and the forebrain areas implicated in motivational control, quality–intensity coding may be highly integrated with hedonic–motivational coding, whereas in the monkey, there may be more distinction[39].

REFERENCES

1 Aleksanyan, Z.A., Buresova, O. and Bures, J., Modification of unit responses to gustatory stimuli by conditioned task aversion in rats, *Physiol. Behav.*, 17 (1976) 173–179.
2 Anand, B.K. and Brobeck, J.R., Hypothalamic control of food intake in rats and cats, *Yale J. Biol. Med.*, 24 (1951) 123–140.
3 Beckstead, R.M. and Norgren, R., An autoradiographic examination of the central distribution of the trigeminal, facial, glossopharyngeal and vagal nerves in the monkey, *J. Comp. Neurol.*, 184 (1979) 455–472.
4 Beckstead, R.M., Morse, J.R. and Norgren, R., The nucleus of the solitary tract in the monkey: projections to the thalamus and brainstem nuclei, *J. Comp. Neurol.*, 190 (1980) 259–282.
5 Bereiter, D.A., Berthoud, H.-R. and Jeanrenaud, B., Oropharyngeal and hypothalamic input to the same NTS neurons, *Soc. Neurosci. Abstr.*, 5 (1979) 396.
6 Burton, M.J., Rolls, E.T. and Mora, F., Effects of hunger on the responses of neurons in the lateral hypothalamus to the sight and taste of food, *Exp. Neurol.*, 51 (1979) 668–677.
7 Cabanac, M., Physiological role of pleasure, *Science*, 173 (1971) 1103–1107.
8 Cabanac, M. and Duclaux, R., Specificity of internal signals in producing satiety for taste stimuli, *Nature (London)*, 227 (1970) 966–967.
9 Covian, M.R. and Antunes-Rodrigues, J., Specific alterations in sodium chloride intake after hypothalamic lesions in the rat, *Am. J. Physiol.*, 205 (1963) 922–926.
10 Covian, M.R., Antunes-Rodrigues, J., Gentil, C.G., Saad, W.A., Camargo, L.A. and Silva-Neto, C.R., Central control of salt balance. In G.J. Mogenson and R.F. Calaresu (Eds.), *Neural Integration of Physiological Mechanisms and Behavior*, University of Toronto Press, Toronto, 1975, pp. 267–282.
11 Gallyas, F., Silver staining of myelin by means of physical development, *Neurol. Res.*, 1 (1979) 203–209.
12 Giza, B.K. and Scott, T.R., Blood glucose selectively affects taste-evoked activity in rat nucleus tractus solitarius, *Physiol. Behav.*, 31 (1983) 643–650.
13 Glenn, J.F. and Erickson, R.P., Gastric modulation of gustatory afferent activity, *Physiol. Behav.*, 16 (1976) 561–568.
14 Goetzl, F.R., Ahokas, A.J. and Payne, J.G., Occurrence in normal individuals of diurnal variations in acuity of the sense of taste for sucrose, *J. Appl. Physiol.*, 2 (1950) 619–626.
15 Goetzl, F.R. and Stone, F., Diurnal variations in acuity of olfaction and food intake, *Gastroenterology*, 9 (1947) 444–453.
16 Grossman, S.P., Role of the hypothalamus in the regulation of food and water intake, *Psychol. Rev.*, 82 (1975) 200–224.
17 Hoebel, B.G., Feeding and self-stimulation, *Ann. N.Y. Acad. Sci.*, 157 (1969) 758–778.
18 Kawamura, Y., Kasahara, Y. and Funakoski, M., A possible brain mechanism for rejection behavior to strong salt solution, *Physiol. Behav.*, 5 (1970) 67–74.
19 Merrill, E.G. and Ainsworth, A., Glass-coated platinum-plated tungsten microelectrodes, *Med. Biol. Eng.*, 10 (1972) 662–672.
20 Mesulam, M.-M. and Mufson, E.J., Insula of the old world monkey. III. Efferent cortical output and comments on function, *J. Comp. Neurol.*, 212 (1982) 38–52.
21 Miller, N.E., Experiments on motivation: studies combining psychological, physiological and pharmacological techniques, *Science*, 126 (1957) 1271–1278.
22 Moskowitz, H.R., Kumraiah, V., Sharma, K.N., Jacobs, L.H. and Sharma, S.D., Effects of hunger, satiety and glucose load upon taste intensity and taste hedonics, *Physiol. Behav.*, 16 (1976) 471–475.
23 Mowrer, G.D., Maire, R.G. and Engen, T., Influence of internal factors on the perceived intensity and pleasantness of gustatory and olfactory stimuli. In M.R. Kare and O. Maller (Eds.), *The Chemical Senses and Nutrition*, Academic Press, New York, 1977, pp. 103–118.
24 Norgren, R., Gustatory responses in the hypothalamus, *Brain Research*, 21 (1970) 63–71.
25 Norgren, R., Gustatory afferents to ventral forebrain, *Brain Research*, 81 (1974) 285–295.
26 Norgren, R., Taste pathways to hypothalamus and amygdala, *J. Comp. Neurol.*, 166 (1976) 17–30.
27 Norgren, R., A synopsis of gustatory neuroanatomy. In J. Le Magnen and P. MacLeod (Eds.), *Olfaction and Taste, Vol. VI*, I.R.L. Press, London, 1977, pp. 225–232.
28 Norgren, R., The central organization of the gustatory and visceral afferent systems in the nucleus of the solitary tract. In Y. Katsuki, R. Norgren and M. Sato (Eds.), *Brain Mechanisms of Sensation*, John Wiley and Sons, New York, 1981, pp. 143–160.
29 Norgren, R. and Leonard, C.M., Taste pathways in rat brainstem, *Science*, 173 (1971) 1136–1139.
30 Norgren, R. and Leonard, C.M., Ascending central gustatory pathways, *J. Comp. Neurol.*, 150 (1973) 217–237.
31 Rolls, B.J., Rolls, E.T. and Rowe, E.A., Sensory specific satiety in man, *Physiol. Behav.*, 27 (1981) 137–142.
32 Rolls, B.J., Rowe, E.A., Rolls, E.T., Kingston, B. and Megson, A., Variety in a meal enhances food intake in man, *Physiol. Behav.*, 26 (1981) 215–221.
33 Rolls, B.J., Rowe, E.A. and Rolls, E.T., How sensory properties of foods affect human feeding behavior, *Physiol. Behav.*, 29 (1982) 409–417.
34 Rolls, E.T., *The Brain and Reward*, Pergamon, Oxford, 1975.

35 Rolls, E.T., Processing beyond the inferior temporal visual cortex related to feeding, learning and striatal function. In Y. Katsuki, R. Norgren and M. Sato (Eds.), *Brain Mechanisms of Sensation*, Wiley, New York, 1981, pp. 241–269.
36 Rolls, E.T., Central nervous mechanisms related to feeding and appetite, *Brit. Med. Bull.*, 37 (1981) 131–134.
37 Rolls, E.T., Feeding and reward. In D. Novin and B.G. Hoebel (Eds.), *The Neural Basis of Feeding and Reward*, Brunswick, Maine: Haer Institute for Electrophysiological Research, 1982.
38 Rolls, E.T., The neurophysiology of feeding, *Int. J. Obesity*, 8 (1984) 139–150.
39 Rolls, E.T., Neuronal activity related to the control of feeding. In R. Ritter and S. Ritter (Eds.), *Neural and Humoral Controls of Food Intake*, Academic Press, New York, 1985.
40 Rolls, E.T., Burton, M.J. and Mora, F., Hypothalamic neuronal responses associated with the sight of food, *Brain Research*, 111 (1976) 53–66.
41 Rolls, E.T. and Rolls, B.J., Activity of neurones in sensory, hypothalamic and motor areas during feeding in the monkey. In Y. Katsuki, M. Sato, S. Takagi and Y. Oomura (Eds.), *Food Intake and Chemical Senses*, University of Tokyo Press, Tokyo, 1977, pp. 525–549.
42 Rolls, E.T., Sanghera, M.K. and Roper-Hall, A., The latency of activation of neurons in the lateral hypothalamus and substantia innominata during feeding in the monkey, *Brain Research*, 164 (1979) 121–135.
43 Rolls, E.T., Burton, M.J. and Mora, F., Neurophysiological analysis of brain-stimulation reward in the monkey, *Brain Research*, 194 (1979) 339–357.
44 Rolls, E.T. and Rolls, B.J., Brain mechanisms involved in feeding. In L.M. Barker (Ed.), *Psychobiology of Human Food Selection*, AVI Publishing Company, Westport, CT, 1982, pp. 33–62.
45 Rolls, E.T., Rolls, B.J. and Rowe, E.A., Sensory-specific and motivation-specific satiety for the sight and taste of food and water in man, *Physiol. Behav.*, 30 (1983) 185–192.
46 Rolls, E.T., Murzi, E., Yaxley, S., Thorpe, S.J. and Simpson, S.J., Sensory-specific satiety: food-specific reduction in responsiveness of ventral forebrain neurons after feeding in the monkey, 1985.
47 Sanghera, M.K., Rolls, E.T. and Roper-Hall, A., Visual responses of neurons in the dorsolateral amygdala of the alert monkey, *Exp. Neurol.*, 63 (1979) 610–626.
48 Saper, C.B., Loewy, A.D., Swanson, L.W. and Gowan, W.M., Direct hypothalamo-autonomic connections, *Brain Research*, 117 (1976) 305–312.
49 Scherr, S. and King, K.R., Sensory and metabolic feedback in the modulation of taste hedonics, *Physiol. Behav.*, 29 (1982) 827–832.
50 Scott, T.R., Yaxley, S., Sienkiewicz, Z.J. and Rolls, E.T., Taste responses in the nucleus tractus solitarius of the behaving monkey, *J. Neurophysiol.*, in press.
51 Stellar, E., The physiology of motivation, *Psychol. Rev.*, 61 (1954) 5–22.
52 Thorpe, S.J., Rolls, E.T. and Maddison, S., Neuronal activity in the orbitofrontal cortex of the behaving monkey, *Exp. Brain Res.*, 49 (1983) 93–115.
53 Wolf, G., Effect of dorsolateral hypothalamic lesions on sodium appetite elicited by desoxycorticosterone and by acute hyponatremia, *J. Comp. Physiol. Psychol.*, 58 (1964) 396–402.
54 Wolf, G. and Quartermain, D., Sodium chloride intake of adrenalectomized rats with lateral hypothalamic lesions, *Am. J. Physiol.*, 212 (1967) 133–148.